

**REMARKS**

Reconsideration is requested.

Claims 1-21, 23, 25 and 28 have been canceled, without prejudice. Claim 32 has been added. Claims 22, 24, 26-27 and 29-32 are pending. No new matter has been added.

The Examiner has objected the specification as allegedly not including a separate section describing the figures. The applicants respectfully submit that the required section is provided in the first paragraph on page 55 of the application. Further correction of the specification should not be required and withdrawal of the objection is requested. The Examiner is requested to advise the undersigned in the event anything further is required in this regard.

The Examiner has objected to the drawings allegedly filed June 16, 2004. The Examiner is believed however to have inadvertently believed that the figures attached to the Declaration of Dr. Shitara were amended figures to be used in place of the originally-filed Figure 1. This was not the applicants intention and the Examiner is requested to have the Patent Office records corrected in this regard in the event the figures attached to the Shitara Declaration have been inserted in to the application as the figures of the application. Withdrawal of the objection to the specification and drawings and acceptance of the drawings of record are requested.

The Section 103 rejection of claims 22-27 and 29-31 have been rejected as allegedly being obvious over Bellamy (Cancer Research 1999 February, 59:728-733), Shitara (U.S. Patent No. 6,617,160) and Rockwell (U.S. Patent No. 5,840,301), is

traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The presently claimed invention relates to a method for treating leukemia, comprising administering a humanized (e.g., human chimeric) anti-human VEGF receptor Flt-1 antibody which has ADCC activity (antibody-dependent cellular cytotoxic activity) against leukemia cells. The antibody of the present invention clearly has ADCC activity against leukemia cells, as shown at page 48, lines 12-17 in the present specification and page 3, line 10 to page 5, line 17 of Dr. Shitara's Declaration submitted on June 16, 2004.

Shitara is understood to disclose a neutralizing antibody against Flt-1, while neither disclosing nor suggesting a humanized anti-Flt-1 antibody having ADCC activity. In Rockwell, only a flk-1 antibody was prepared, but such a humanized anti-Flt-1 antibody having ADCC activity was not actually prepared. That is, the antibodies disclosed in Shitara and Rockwell may be able to inhibit signal transduction of VEGF, but they cannot injure the leukemia cells. Furthermore, Bellamy discloses that the leukemia cells express bFGF as well as VEGF (page 731, right column, second paragraph in DISCUSSION) and IL-6 is an important factor for the proliferation of leukemia (page 732, right column, first full paragraph). Accordingly, although the antibodies of Shitara and Rockwell can inhibit signal transduction of VEGF in leukemia cells, they cannot inhibit signal transduction of factors which are different from VEGF, such as bFGF and IL-6. The combination of references would not have led one of ordinary skill in the art to make the presently claimed invention.

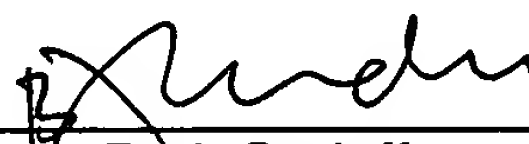
The Examiner is urged to appreciate that the present invention provides, for the first time, complete inhibition of the proliferation of leukemia cells using the humanized anti-Flt-1 antibody which has ADCC activity against leukemia cells. Accordingly, even if Bellamy were combined with Shitara and Rockwell, leukemia could not have been treated in a manner presently claimed. The claimed invention would not have been obvious from the combination of cited art. Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

**NIXON & VANDERHYTE P.C.**

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